

(11) **EP 0 379 156 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention
of the grant of the patent:
10.04.1996 Bulletin 1996/15

(51) Int Cl.⁶: **C08J 7/04, C09D 201/08,
A61L 29/00, B05D 5/08**

(21) Application number: **90100854.0**

(22) Date of filing: **16.01.1990**

(54) **Improved hydrophilic lubricious coatings**

Hydrophile gleitfähige Beschichtungen

Revêtements hydrophiles lubrifiés améliorés

(84) Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

(30) Priority: **17.01.1989 US 297331**
22.12.1989 US 449777

(43) Date of publication of application:
25.07.1990 Bulletin 1990/30

(73) Proprietor: **UNION CARBIDE CHEMICALS AND
PLASTICS COMPANY INC.**
(a New York corporation)
Danbury Connecticut 06817-0001 (US)

(72) Inventor: **Fan, You-Ling**
East Brunswick 08816 (US)

(74) Representative: **Barz, Peter, Dr. et al**
Patentanwalt
Kaiserplatz 2
D-80803 München (DE)

(56) References cited:
EP-A- 0 010 621 CH-A- 340 261
US-A- 4 729 914

Remarks:

The file contains technical information submitted
after the application was filed and not included in
this specification

BEST AVAILABLE COPY

EP 0 379 156 B1

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Description

This invention relates in general to a method of coating substrates. In one aspect, this invention is directed to the coating of medical devices and other substrates to provide them with improved lubricious coatings. In a further aspect, said method provides medical devices, such as catheters, guide wires and the like, which when dry exhibit little or no lubricity but when moistened, possess a lubricity which aids in moving the devices within the body with ease and little discomfort. In another aspect, this invention is directed to a process for the preparation of the coated medical devices which are useful in the diagnosis or treatment of various conditions in the human body.

Catheters which are used surgically for insertion through blood vessels, urethra, or body conduits, and guide wires used with catheters for biopsy, balloon angioplasty and other medical procedures require a low-friction surface for preventing injury to, or inflammation of, mucous membranes and other body tissues.

One class of conventional catheters is made of low-friction materials such as Teflon®, polyethylene or other materials coated with a layer of Teflon® or silicone. There are two shortcomings of these catheters: First, they are not sufficiently slippery for the intended surgical purposes mentioned above. Second, they are difficult to handle and store because their surfaces are slippery at all times.

Another class of conventional catheters is rendered lubricious by coating with a layer of silicone fluid, glycerin, or olive oil. These materials are unsatisfactory because the low molecular weight additives tend to run off quickly. Thus, they lose the initial lubricity rather rapidly.

Another class of conventional surface treatment involves the deposition of poly(vinyl pyrrolidone) in the presence of a polyisocyanate. This type of coating while lubricious initially lacks abrasion resistance, and is therefore easily removed from the surface of the medical devices. An improved version of this technique was described in US-A-4,373,009 and 4 729 914, where an active hydrogen containing vinyl pyrrolidone copolymer was used instead to result in a better bonding to the substrate. The "monomers containing active hydrogen" were needed "to form a covalent bond between the coupling coating and the hydrophilic copolymer". These copolymers, however, were of unknown quality in terms of purity, toxicity, or not of sufficiently high molecular weight needed for this application. Both the availability and usefulness of these copolymers are highly questionable.

in US-A-4,119,094, a substrate such as a tube or catheter is disclosed having a hydrophilic coating which exhibits a low coefficient of friction. The substrate is coated with a poly(vinyl pyrrolidone)-polyurethane interpolymers. A polyisocyanate and a polyurethane mixture is applied to a substrate and after drying, a poly(vinylpyrrolidone) in solution is applied.

US-A-4,589,873 discloses a method of applying a hydrophilic coating to a polymeric substrate. The coating consists of poly(vinyl pyrrolidone) which is applied to the substrate in a solvent followed by drying.

US-A-4,642,267 discloses and claims a hydrophilic polymer blend. The blend is comprised of a thermoplastic polyurethane having no reactive isocyanate groups and a hydrophilic poly(N-vinyl lactam) such as poly(vinyl pyrrolidone). The blend can contain additional polymeric components such as homopolymers or copolymers of monomers including vinyl chloride, acrylic acid, vinyl alcohol and the like.

A process for coating a polymer surface with a hydrophilic coating is also disclosed in US-A-4,666,437. A solution of a compound containing at least two unreacted isocyanate groups per molecule is applied to the polymer surface and the solvent evaporated. Thereafter, a solution of poly(vinyl pyrrolidone) is applied to the treated surface and the coated cured.

EP-A-166998, describes lubricious coatings derived from either a cellulosic polymer, a maleic anhydride polymer, a polyacrylamide or a water-soluble nylon which are covalently bonded to a medical instrument substrate. The substrate contains reactive functional groups such as aldehydes, epoxy, isocyanate or amino groups. The reference indicates that the water soluble polymers are non-crosslinked and contain hydrophilic groups such as -OH, -CONH₂, -COOH, -NH₂, -COO⁻, -SO₃⁻, and -NR₃, R being alkyl or hydrogen. However, a cellulosic polymer is undesirable because it must be protected against microbe attack. Coatings made from a maleic anhydride polymer must go through a tedious post treatment with water before developing lubricity, while water-soluble nylons may have questionable stability.

CH-A-340261 is directed to a method of rendering electrically non-conductive substrates antistatic by coating said substrates sequentially with an aqueous solution of poly(acrylic acid) and an aqueous solution of a cation-active substance such as a quaternary ammonium compound.

It has now unexpectedly and surprisingly been found that certain high molecular weight poly(carboxylic acids) or their partially neutralized salts, can be strongly bonded to a substrate, such as a catheter, using a polyisocyanate reagent and at the same time provides a hydrophilic lubricious coating. Thus, the need for either an interpenetrating network containing poly(vinyl pyrrolidone) and polyurethane or a copolymer containing both non-active hydrogen units and active-hydrogen units can be avoided. Furthermore, there is no need for any post hydrolysis treatment in the invention. Unlike a maleic anhydride polymer, the coating develops lubricity instantly upon exposure to an aqueous fluid. Poly(acrylic acids), such as the Carbopol® brands manufactured by B.F. Goodrich, are ideally suited for the intended medical applications, and also have sufficiently high molecular weights necessary for achieving both good hydrophilic lubricity

and abrasion resistance.

Accordingly, one or more of the following objects will be achieved by the practice of this invention. It is an object of this invention to provide medical and other devices which when dry do not exhibit a slippery surface, but when contacted with a fluid such as water, become very lubricious. Another object of this invention is to provide medical and other devices which are easily handled without fear of slipping, but when moistened or contacted with body fluids instantly become very lubricious. A further object of this invention is to provide medical devices having a coating of a poly(carboxylic acid) and a polyisocyanate which when dried can be handled with ease, but when moistened, become very slippery.

The present invention provides a method of covering at least a portion of a substrate with a hydrophilic coating having good abrasion resistance and which exhibits an increased lubricity when contacted with an aqueous-containing fluid, said method comprising the steps of:

- (1) contacting said substrate with a polyisocyanate or end-capped prepolymer or adduct thereof dissolved or dispersed in at least one first inert solvent to provide an at least partially coated substrate;
- (2) contacting said coated substrate with a poly(carboxylic acid) specified hereinafter, said poly(carboxylic acid) being dissolved or dispersed in at least one second inert solvent to provide a multiple coated substrate; and
- (3) thereafter drying said multiple coated substrate to provide a hydrophilic, lubricious coating.

One or more polyisocyanates is applied to a substrate such as a medical device. The contact time may vary from a few seconds to an hour or more depending upon the material of construction of the medical device and the polyisocyanate employed. The primer coated medical device can be dried in an oven for removal of any solvent and then the poly(carboxylic acid) top coat can be applied directly to the polyisocyanate coated device. The coated medical device is then dried to complete the coating process. The finished medical device has normal feel and handling characteristics when dry. Upon exposure to body fluids, however, it becomes lubricious instantly.

The hydrophilic lubricious coating of this invention is prepared by first contacting a substrate or medical device, such as a catheter, with a polyisocyanate such as a toluene diisocyanate in a liquid medium. The liquid medium can be removed by drying or the catheter can be treated directly with the high molecular weight poly(carboxylic acid) in a liquid medium. After drying in an oven, a non-tacky, easy-to-handle, and uniformly coated catheter is obtained. The surface of the resultant catheter becomes lubricious instantly upon exposure to an aqueous solution or body fluids.

In addition to a quick initial lubricity, the hydrophilic lubricious coating of this invention is resistant to abrasion. Consequently, a catheter coated in accordance with the teachings of this invention will retain a lubricious surface for a long duration which is often required during the course of a surgical procedure.

Unlike catheters made of or coated with Teflon® or silicones, catheters coated in accordance with the present invention are non-slippery when dry but become instantly slippery when wet. As a result, medical devices coated with the hydrophilic lubricious coatings of this invention are easier to handle and store.

The term "bath" as employed throughout the specification and appended claims is meant to include not only solutions of the indicated organic compounds, but also dispersions, e.g. emulsions, thereof.

Application of the coatings from the bath can be effected by a variety of methods and includes, but is not limited to, dipping, spraying, electrical deposition and painting. Optionally, the coated substrate can be further treated with an aqueous bath to partially or totally neutralize the free acid. In those instances wherein the substrate is subjected to high temperatures, such as in thermoforming processes, the treatment with the aqueous bath to effect neutralization or partial neutralization is desired.

As indicated above, the hydrophilic lubricious coating of this invention is comprised of at least two components; a polyisocyanate primer and a water-soluble or water dispersible poly(carboxylic acid) topcoat. They are normally applied in two separate coating steps. However, if desired, the drying step after application of the polyisocyanate coating can be omitted and drying effected after application of the top coat.

The solvents useful for applying the polyisocyanates include methyl ethyl ketone, ethyl acetate, ethyl lactate, chloroform, trichloroethylene, dichloromethane, hexane, heptane, toluene, their mixtures with mineral oil, or other suitable organic solvents which do not react with isocyanates under the coating conditions. The preferred solvent is methyl ethyl ketone.

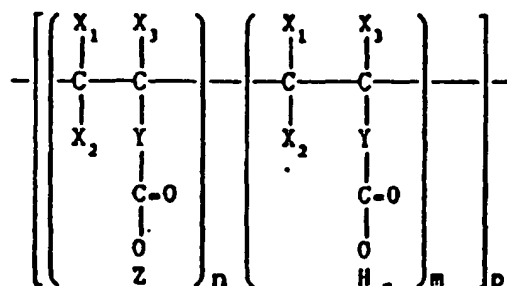
Alternatively, the polyisocyanates can be dispersed in a solvent/non-solvent mixture to form a dispersion, for instance, emulsified to form an oil-in-water emulsion. When an emulsion is used, the reactive isocyanate groups need to be protected by suitable chemical groups known to those skilled in the art.

A wide variety of polyisocyanates can be employed in preparing the coatings of the present invention and include, but are not limited to, toluene-2,3-diisocyanate, toluene-2,6-diisocyanate, commercial mixtures of toluene-2,4- and 2,6-diisocyanates, 4,4'-diphenylmethane diisocyanate, cyclohexylene-1,4-diisocyanate, m-phenylene diisocyanate, 3,3-diphenyl-4-biphenylene diisocyanate, 4,4-biphenyl diisocyanate, 1,6-hexamethylene diisocyanate, 1,5-naphthalene diisocyanate, cumene-2,3-diisocyanate, 2,4-diisocyanatodiphenylether, 5,6-dimethyl-1,3-phenylenediisocyanate, 2,4-dimethyl-1,3-phenylenediisocyanate, 2,4-dimethyl-1,3-phenylenediisocyanate, 4,4-diisocyanatodiphenylether,

9,10-anthracene diisocyanate, 2,4-diisocyanatotoluene, 1,4-anthracene diisocyanate, 2,4,6-toluene triisocyanate, isophorone diisocyanate, and p,p',p"-triphenylmethane triisocyanate. Equally useful are isocyanate end-capped prepolymers and adducts, isocyanate end-capped polyfunctional aromatic adducts, isocyanate end-capped polyfunctional aliphatic adducts and two component systems such as end-capped aliphatic polyester polyol and aliphatic polyol compounds, and their mixtures with different polyisocyanates as described above.

Illustrative of isocyanate end-capped adducts are the reaction products of 2,4-tolylene diisocyanate, 4,4'-diphenylmethane diisocyanate, polymethylenepolyphenyl isocyanate, or 1,5-naphthylene diisocyanate, with 1,2-polypropylene glycol, polytetramethylene ether glycol, 1,4-butanediol, 1,4-butylene glycol, 1,3-butylene glycol, poly(1,4-oxybutylene) glycol, caprolactone, adipic acid esters, phthalic anhydride, ethylene glycol and diethylene glycol.

The polymers used for forming the top coatings of the present invention are poly(carboxylic acids) in the free acid or partially neutralized forms as represented by the following formula:



where

$n = 0-0.95$ mole fraction of neutralized acid moieties;

$m = 0.05-1.0$ mole fraction of acid moieties with the proviso that $n+m = 1$;

X_1, X_2, X_3 are each a hydrogen atom or a suitable monovalent organic radical, such as lower alkyl or cycloalkyl or aryl of up to 8 carbon atoms, and wherein the X groups are such that the polymer remains water soluble;

Y is either a single bond or any suitable divalent organic radical, such as a hydrocarbon group of up to 8 carbon atoms, provided it does not adversely affect the solubility of the polymer;

Z is either a metallic ion or a tertiary ammonium ion; and

p is a very large number such that the polymer has a molecular weight between 200,000 and 5,000,000.

Representative poly(carboxylic acid) homopolymers include, but are not limited to, poly(acrylic acid), poly(methacrylic acid) and poly(isocrotonic acid). The poly(carboxylic acid) of this invention can be either linear or partially cross-linked such that it would form either a solution or a colloidal dispersion in the coating medium. The preferred poly(carboxylic acid) polymer is a poly(acrylic acid) having a molecular weight of from 200,000 to 5,000,000. Particularly preferred poly(carboxylic acid) polymers include poly(acrylic acid) polymers having molecular weights of from 1,000,000 to 3,000,000.

Copolymers containing water-insoluble units as well as carboxylic acid units can be mixed with the above homopolymers if so desired, as long as they are compatible.

Any organic solvents or mixed solvents for the poly(carboxylic acid) polymers used in this invention may be employed for making the topcoat solution provided that they are not reactive with the polyisocyanates. Exemplary solvents or solvent mixtures include acetonitrile, acetonitrile-DMF, N,N-dimethyl formamide (DMF), acetyl acetone, acrylonitrile, benzonitrile, diethyl acetamide, diethyl formamide, diethylformamide-DMF, dimethyl acetamide, 1,4-dioxane, dipropyl sulfone, DMF-acetone, DMF-toluene, DMSO (dimethyl sulfoxide), DMSO-DMF, ethyl formamide, N-methyl-2-pyrrolidone, nitrobenzene, nitrobenzene-DMF, phenylacetate, propionitrile, and styrene. The dissolution of poly(carboxylic acid) polymers in many of the above-mentioned solvents may be enhanced by the addition of suitable amines. The preferred solvent is dimethyl formamide.

To prepare a seed-free poly(carboxylic acid) solution, it is advantageous to add a small amount of surfactant in the solvent before mixing with the polymer. Any soluble surfactant or a mixture of surfactants in the above-mentioned solvents may be useful. The preferred surfactants are soluble non-ionic surfactants such as polyoxyethylene sorbitan fatty acid esters, polyoxyethylene acids, polyoxyethylene alcohols, fluorinated alkyl esters, fluorinated alkoxylates and their mixtures.

Due to the high molecular weight of the poly(carboxylic acid) polymers used in the present invention, their solution viscosities may be too high to be suitable for some coating processes. It is advantageous in these instances to convert the polymer solution to a colloidal dispersion by mixing with one or more non-solvents. Exemplary non-solvents include

tertiary alcohols, ketones, aliphatic ethers, aliphatic and aromatic hydrocarbons. The preferred non-solvents are acetone, MEKY and tertiary butyl alcohol.

For some applications it might be desirable to incorporate one or more additives in the coatings, particularly the top coating. For example, some catheters are comprised of a thermoplastic rubber and it is preferred that the primer coating contain a plasticizer to minimize loss of flexibility due to the coating operation. A wide variety of plasticizers can be employed such as the esters of fatty acids, mineral oil or silicone oil. The plasticizer must, of course, be compatible with the components of the coatings and have no undesirable biological properties which would limit their use.

Other additives can be employed in the coatings in addition to the surfactants such as, stabilizers, antioxidants, antimicrobial agents, colorants and biological components. For example, in catheters which are inserted into blood vessels, it may be desirable to have contained in the coating an antithrombogenic agent such as heparin, to avoid blood clot formation during the surgical procedure. The antithrombogenic agent can be used either as an additive or as a chemically bonded moiety of the poly(carboxylic acid) polymer.

The techniques employed in coating the substrates and devices are not necessarily critical and any coating processes suitable for making thin coatings may be utilized.

In practice it has been found that excellent lubricity and abrasion resistance properties are obtained when the total thickness of the primer and top coating applied to the substrates in accordance with the teachings of this invention is from the sub- μm range to a few μm .

The concentration of the isocyanate and the poly(carboxylic acid) in the respective coating solutions can vary depending upon the particular components employed, their solubility as well as other considerations. In general the polyisocyanate component in the primer coating is contained in the coating solvent in an amount of at least 0.1% by weight. In practice, it is preferred to employ the polyisocyanate in a solvent in a concentration of from 0.5 to 20% by weight, and more preferably from 1 to 5% by weight.

The amount of the poly(carboxylic acid) component employed in the solvent will be controlled by the viscosity of the medium. Almost any concentration can be used as long as it is high enough to permit the preparation of a satisfactory coating, and yet is low enough so that the solution is not too viscous. Concentrations of from 0.1 to 10% by weight are preferred, a concentration within the range of 0.5 to 2% by weight being the most preferred. In practice, the stoichiometry is such that the molar ratio of carboxylic acid groups to isocyanate groups is greater than 1 and will generally be at least 1:1.

Although the drying temperatures and times are not necessarily critical, it has been found that the coated substrate can be dried at temperatures of from 20 to 150°C and more preferably from 50 to 100°C. Drying periods can range from a few seconds to 60 minutes or more.

Many types of catheters need to be thermoformed to specific shapes for their intended applications. Depending on the temperature and length of time of the thermoforming process many coated catheters may lose their hydrophilic lubricity during the thermoforming process. The degree of lubricity loss depends on the severity of the thermoforming conditions.

Thus, when the temperatures are sufficiently high lubricity may be decreased due to the cyclization of adjacent acid groups. Accordingly, it is preferred to neutralize or partially neutralize the acid groups to prevent such cyclization. The description of treatment of the acid groups by sodium phosphates and preferred formulations are set forth in the examples.

The hydrophilic lubricious coatings of this invention are useful in coating medical devices, where a slippery exterior and/or interior, are necessary or desirable to minimize injury to tissues and to aid in manipulation of the devices during surgical procedures. Exemplary medical devices include catheters, needles, guide wires, prophylactic devices, delivery systems, filters, sheaths, and other accessories employed in medical diagnostics, drainage, dilatation occlusion, vena cava and the like. While the invention is particularly applicable to medical devices, it can also be used to coat a variety of other substrates. For instance, the coatings can be applied to condoms, skis, toboggans, and in those instances wherein a lubricious surface is desired.

In the examples which follow, certain abbreviations have been employed to define the various polyisocyanates and poly(carboxylic acids). All of the compounds are readily available from commercial sources.

Polyisocyanate Composition

A- 1,6-diisocyanatohexane

B- 2,4-toluene diisocyanate

D- An isocyanate end-capped aliphatic prepolymer having an average NCO equivalent weight of 350 and a solution viscosity of about 1,000 mPa-s (cps) at 25°C.

E- An aromatic isocyanate end-capped prepolymer, average NCO equivalent weight 182.

Poly(carboxylic acid) Composition

- 5 L- A poly(acrylic acid) partially cross-linked homopolymer having a molecular weight of about 3,000,000.
M- A USP grade poly(acrylic acid) partially cross-linked homopolymer having a molecular weight of about 3,000,000.
N- A poly(acrylic acid) homopolymer having a molecular weight of about 1,250,000.

10 The following examples in which all percentages are given by weight are illustrative of the invention:

Example 1

15 A nylon 6 coupon was compression molded from Capron® 8000 (Allied Chemicals). The coupon was first dipped into a 1% solution of 1,6-diisocyanatohexane (A) in methyl ethyl ketone (MEK) for one hour. The coupon was subsequently removed from the MEK bath and dried in a 60°C air oven for 30 minutes. The dried coupon was then dipped in a 1% solution of poly(acrylic acid) (L) in dimethylsulfoxide (DMSO) for one second. It was redried at 60°C in an air oven for 30 minutes. The finished coating was smooth, non-lacky, as well as easy to handle. It became instantly slippery upon exposure to water.

Example 2

20 The coated nylon 6 coupon was soaked in a water bath for three hours at room temperature. The soaked coupon retained a high degree of lubricity. This experiment shows that the poly(acrylic acid) coating was held tightly onto the nylon 6 substrate and was not leached out during the soaking.

Example 3

25 A nylon 11 coupon was compression molded from RISAN BESNO®-545344. The coupon was treated according to the same procedure as described in Example 1. The finished coating on the nylon 11 coupon became lubricious instantly upon exposure to water.

Example 4

30 The coated nylon 11 coupon was soaked in a water bath for three hours at room temperature. The soaked nylon 11 coupon remained highly lubricious. This experiment illustrates that the poly(acrylic acid) coating was not dissolved away during the soaking.

Example 5

35 Example 1 was repeated with the exception that N,N-dimethyl formamide (DMF) was substituted for DMSO as the solvent for the poly(acrylic acid). A very lubricious coating was obtained when exposed to water.

Example 6

40 Example 5 was repeated with the exception that the concentration of the poly(acrylic acid) was 0.5 instead of 1%. The finished coating was slightly more smooth and become lubricious upon exposure to water.

Example 7

45 Example 6 was repeated with the exception that (1) an 0.2% poly(acrylic acid) solution was used and (2) the acid polymer was partially neutralized by adding a 50% stoichiometric amount of triethylamine. A smooth coating was obtained which became lubricious upon exposure to water.

Example 8

50 A nylon 11 coupon was compression molded from bismuth carbonate filled nylon 11 pellets. The coupon was coated in a 1% solution of toluene 2,4-diisocyanate (B) in MEK for one hour. After drying in an air oven at 60°C for 30 minutes, the coupon was dipped in a 1% solution of poly(acrylic acid) (L) in dimethylformamide (DMF). After redrying at 60°C for

30 minutes, a smooth coating was obtained. The surface of the coupon became lubricious instantly upon exposure to water.

Example 9

A surgical catheter made of bismuth carbonate filled nylon 11 was coated by the same procedure as described in Example 8 with the exception that poly(acrylic acid) (M) was substituted for (L). The finished catheter had a continuous, smooth coating which became very lubricious upon exposure to water.

Example 10 (comparative)

(a) Example 9 was repeated with the exception that a 1% solution of a (vinyl methyl ether-maleic anhydride) copolymer (GANTREZ-AN® 169 produced by GAF) in MEK was substituted for the poly(acrylic acid) solution as the topcoat. The freshly prepared coating showed no lubricity upon exposure to water. It became lubricious, however, after overnight soaking in a water bath. This example illustrates a deficiency of the prior technique described in EP-A-166998.

(b) A nylon 11 catheter was coated by dipping in a 1 % DMF solution of polyisocyanate (B) for 1 hour after which it was dried at 60°C for one hour. the catheter was then dipped in a 1 % DMF solution of polyvinyl hydrophthalate for 1 second and dried 30 minutes at 60°C. Upon dipping in water there was no development of a lubricious coating.

Example 11

Example 9 was repeated with the exception that 1,6-diisocyanatohexane (A) was substituted for toluene 2,4-diisocyanate (B) in the primer solution. A smooth coating was obtained which became slippery instantly upon exposure to water.

Example 12

Example 9 was repeated with the exception that an isocyanate end-capped polyfunctional aliphatic adduct (D) was substituted for toluene diisocyanate. The isocyanate solution was made of 2.03 grams of (D) and 150 grams of MEK which resulted in an 0.8% solution of (D). The finished coating was continuous and smooth, which developed lubricity immediately upon exposure to water.

Example 13

Example 12 was repeated with the exception that an (ethylene-vinyl acetate) copolymer catheter was substituted for the nylon 11 catheter. The coated catheter showed no discoloration and was smooth. It developed lubricity instantly upon exposure to water.

Example 14

A section of the coated catheter prepared in example 12 was examined for lubricity retention in a saline solution (0.5% NaCl). The following observations were noted and are set forth in Table I below:

TABLE I

Soaking time, hours	Observation
1/6	remained lubricious
1/2	remained lubricious
1	remained lubricious
24	remained lubricious
After redrying at 60°C	normal feel
Exposed to saline again	remained lubricious

These results demonstrate that the hydrophilic lubricious coating of this invention is resistant to saline.

Example 15

Two coated nylon 11 catheters, one taken from example 9 and the other from example 12, were immersed in a hot water bath at 70°C and examined for any loss of lubricity. The results obtained are set forth in Table II below:

TABLE II

Time in 70°C Bath, hours	Observation
0	lubricious
1	lubricious
2	lubricious
3	lubricious
4	lubricious

It is evident from the above data that the coating of the present invention demonstrated a good retention of lubricity in hot water at 70°C.

Example 16

This example illustrates a preferred method for making a uniform solution of poly(acrylic acid) (M) in DMF or similar solvents. Such a solution is easier to handle, filters more rapidly and results in a more uniform coating.

A total of 180 grams of DMF and 0.09 grams of Tween® 80 [poly(oxyethylene) (20) sorbitan monooleate, a non-ionic surfactant supplied by ICI] were placed in a 500 ml beaker. The mixture was blended for 5 minutes using an air-driven Cowles mixer. Thereafter, 1.8 grams of (M) was sprinkled into the liquid while under mixing. The mixing was continued for a total of 15 minutes. A highly uniform, gel-seeds-free solution was obtained, the finished solution exhibited a Brookfield viscosity (Model LVT, 6 RPM at 25°C) of 55 mPa·s (cps). The dissolution process was much more time-consuming without the surfactant, and the finished solution typically exhibited a viscosity of about 100 mPa·s (cps).

Example 17

Example 16 was repeated with the exception that BRIJ® 98 [polyoxyethylene (20) oleylether, a non-ionic surfactant produced by ICI] was substituted for the Tween® 80. A uniform gel-seed-free solution was obtained. The solution was filtered through a 16 µm filter with ease. The finished solution exhibited a Brookfield viscosity of 45 mPa·s (cps).

Example 18

Example 17 was repeated with the exception that MYRJ® 53 [polyoxyethylene (50) stearate, a non-ionic surfactant produced by ICI] was substituted for BRIJ® 98. A uniform, gel-seed-free dispersion was obtained. The dispersion filtered through a 16 µm filter with ease. The finished dispersion exhibited a Brookfield viscosity of 45 mPa·s (cps) (Model LTV, 6 rpm at 25°C).

Example 19

A stainless steel guide wire made by Medi-tech was coated with a primer solution composed of 1% polyisocyanate (D) in MEK and a topcoat solution composed of 1% poly(acrylic acid) (M) and 0.05% of MYRJ® 53 (surfactant) in DMF. The drying cycles used for the two coats were 30 minutes at 70°C and 30 minutes at 60°C, respectively. The finished stainless steel guide wire showed a lubricious surface upon exposure to water.

Example 20

A bismuth carbonate filled nylon 11 catheter was first dipped in a 1% tolylene-2,4-diisocyanate solution in MEK for one hour. The catheter was removed from the bath and dried in an air oven at 90°C for 30 minutes. It was dipped-coated in a poly(acrylic acid) (M) dispersion having a formulation identical to that of example 18 for 1 second. The catheter was redried at 90°C for 30 minutes. The finished coating was very lubricious and showed a high degree of abrasion resistance.

Example 21

A nylon 11 catheter was coated by first treating it in a primer solution containing 0.5% and 0.5% of polyisocyanate (D) and tolylene 2,4-diisocyanate, respectively. The catheter was dried at 85°C for 30 minutes and subsequently dipped in a 1% poly(acrylic acid) (L) dispersion for one second. It was then redried at 85°C for 30 minutes. The finished catheter was smooth, and showed a high degree of lubricity upon exposure to water. The hydrophilic lubricious coating on this catheter was resistant to abrasion, and retained much of its initial lubricity after rubbing with a wet tissue ten times.

Example 22

A nylon 11 catheter was coated according to the same procedure as described in example 21 with the exception that the ratio of tolylene 2,4-diisocyanate to (D) was changed from 0.5/0.5 to 0.75/0.25. The finished catheter was very lubricious upon exposure to water. It exhibited good abrasion resistance as measured by the rub test described in example 21.

Example 23

A catheter was coated according to the procedure of example 22 with the exception that the drying temperature was 60 instead of 85°C. The finished catheter was very lubricious upon exposure to water.

Example 24

A double-coating procedure is illustrated in this example. Five pieces of nylon 11 catheters were first soaked in a 1% tolylene 2,4-diisocyanate solution in MEK for one hour. After 30 minutes drying in an air oven at 85°C., they were dipped-coated in a 1% poly(acrylic acid) (M) solution for one second. They were redried at 85°C for 30 minutes. The above coating procedure was repeated once more with the exception that the dipping time in the primer solution was shortened from one hour to 10 minutes for the second coating. The finished catheters were very slippery upon exposure to water.

Example 25

A low viscosity, uniform colloidal dispersion of poly(acrylic acid) (N) [a high molecular weight linear poly(acrylic acid)] was prepared by the following procedure: Ten grams of (N) were added under mixing with a Cowles air mixer to a solution containing 0.5 grams of MYRJ® 53 surfactant and 659.7 grams of DMF. A viscous solution was obtained in about 15 minutes. Thereafter, 32.98 grams of MEK were added into the solution under mixing to yield a slightly cloudy colloidal dispersion. The colloidal dispersion possessed a Brookfield viscosity (Model LVT, 6 rpm at 25°C) of 162 mPa-s (cps). Without MEK, a 1% (N) solution in DMF would produce a viscosity of 2,300 mPa-s (cps).

Example 26

A nylon 11 catheter was coated using the procedure described in example 21 with the exception that the primer solution was a 1% tolylene 2,4-diisocyanate solution in MEK and the top coat solution was a 1% poly(acrylic acid) (N) solution in DMF prepared in accordance with example 24. The finished coating was very smooth and became lubricious instantly upon exposure to water.

Example 27

A bismuth carbonate filled nylon 11 catheter was coated with a hydrophilic lubricious coating by the following procedure:

- (1) Dipped in an 1% tolylene 2,4-diisocyanate solution in MEK for one hour.
- (2) Dried in an air oven at 85°C for 30 minutes.
- (3) Dipped in a 1% poly(acrylic acid) ((L)) solution for one second.
- (4) Dried in an air oven at 85°C for 30 minutes.
- (5) Repeated (1) except for 10 minutes.
- (6) Repeated (2).
- (7) Repeated (3).
- (8) Repeated (4).

EP 0 379 156 B1

The finished coating was smooth and continuous. It became very slippery instantly upon exposure to water and showed a good abrasion resistance by the tissue paper rub test.

Example 28

Example 27 was repeated with the exception that a nylon 12 catheter was substituted for the nylon 11 catheter. The finished coating was lubricious and exhibited good abrasion resistance.

Example 29

A catheter made of thermal plastic rubber Kraton® was coated according to the following procedure:

(1) Dipped in a bath containing a primer solution of the following composition

Tolyene diisocyanate	0.75%
Isocyanate (D)	0.25%
Mineral Oil	15%
DMF	84%

for one minute duration.

(2) Dried in an air oven at 85°C for 30 minutes.

(3) Dipped in a 1.5% poly(acrylic acid) (M), solution in DMF for one second.

(4) Dried in an air oven at 85°C for 30 minutes.

The finished catheter retained its flexibility, showed negligible shrinkage, and a smooth coating. The latter became very lubricious upon exposure to water and was resistant to abrasion.

Example 30

A catheter made of poly(ethylene/vinyl acetate) was coated according to the following procedure:

(1) Dipped in a 1% isocyanate (D) solution in MEK for 30 minutes.

(2) Dried at 60°C for 30 minutes.

(3) Dipped in a 1.5% poly(acrylic acid) (M) solution in DMF for one second.

(4) Dried at 60°C for 30 minutes.

(5) Repeated (1) but for 10 minutes.

(6) Repeated (2).

(7) Repeated (3).

(8) repeated (4).

The finished catheter was very smooth and retained its original whitish color. It became lubricious instantly upon exposure to water. The coating was practically unaffected after 10 rubs with a wet tissue paper.

Example 31

A 15 cm (6-inch) tip of a guide catheter wire used in conjunction with a catheter was coated using the procedure described in the previous examples. The guide wire was dipped in a primer solution containing 1.0% isocyanate (D) in MEK and dried for 10 minutes at 85°C. The wire was subsequently dipped in a 1.5% poly(acrylic acid) (M) solution in DMF for 1 second and redried. The coated guide wire showed a good degree of lubricity and retained much of its initial lubricity after rubbing with a wet tissue 4 times.

Example 32

Example 31 was repeated on the full length of the guide wire using a 7:3 DMF/MEK solvent for the poly(acrylic acid) and the sequence of coating was repeated a second time. The coated guide wire exhibited a good degree of lubricity upon exposure to water.

Example 33

5 The full length of a nylon 11 catheter comprised of a polyether thermoplastic elastomer and fitted with a polyethylene terephthalate balloon was coated in a manner similar to the preceding examples. The catheter including the balloon was dipped in a primer solution containing 1% isocyanate (D) in MEK and dried for 30 minutes at 85°C. The catheter with balloon was subsequently dipped in a 1.5% poly(acrylic acid) (L) dispersion (7:3 DMF/MEK) for 1 second and dried. The catheter showed very good lubricity upon exposure to water and retained much of its initial lubricity after rubbing 8 times with a wet tissue.

Examples 34-57

10 Additional experiments were conducted to evaluate various catheters coated in accordance with the present invention and wherein variations were made in coating compositions, solvents, number of coatings, drying times and the like. The pertinent data is set forth in Tables I-III below.

TABLE I
PREPARATION AND EVALUATION OF
ETHYLENE-VINYL ACETATE-COPOLYMER CATHETER

Example(1)	Primer Coating(2)		Top Coating(3)		Evaluation	
	Isocyanate	Weight (g)	Solvent	Acid Compound	Weight & Solvent *	Abrasion Lubricity
34	2,4-TDI (D)	0.5 0.5	MEK	(M)	1.0 DMF	good good
35	(D)	1.0	MEK	(M)	1.0 DMF	good good
36	TDI (D)	0.25 0.75	MEK	(M)	1.0 DMF	good good
37	2,4-TDI (D)	0.75 0.25	MEK	(M)	1.0 DMF	good good
38	2,4-TDI (D)	0.75 0.25	MEK	(M)	0.75 0.25 DMF	good good
39**	(D)	1.0	MEK	(N)	1.0 DMF	good good
40**	(D)	1.0	MEK	(M)	1.0 DMF	good good
41	(D)	1.0	MEK	(M)	1.0 DMF	good good

(1) The ethylene vinyl acetate catheters were 10cm(4 inches) in length.

(2) The catheters were soaked for 60 minutes and dried at 65°C.

(3) The catheters were dipped for 1 second and dried at 65°C.

* Also contained MYRJ®53 surfactant.

** Entire catheter coated and coating sequence repeated.

TABLE II
PREPARATION AND EVALUATION OF
FLEXIBLE THERMOPLASTIC RUBBER CATHETER

Example (1) Catheter	Primer Coating (2)		Top Coating (3)		Evaluation		
Size cm (inch)	Isocyanate	Weight (%)	Solvent	Acid Compound	Weight %	Solvent	Abrasion lubricity
42 10(4) 2,4-TDI (D)	0.75 0.25		MEK	(M)	1.5	DMF/MEK (7:3)	18 (rubs) good
43 30(12) TDI (D)	0.75 0.25		MEK	(M)	1.5	DMF/MEK (7:3)	18 good
44 30(12) TDI (D)	0.75 0.25		MEK	(M)	1.5	DMF/MEK (7:3)	21 good
45 30(12) 2,4-TDI (D)	0.75 0.25		MEK	(M)	1.5	DMF/MEK (1:1)	9 good
46*full (D)	1.05		MEK	(M)	1.0	DMF	20 good
47 10(4) (D)	1.0		MEK	(M)	1.0	DMF	10 good
48 half (D)	1.0		MEK	(M)	1.0	DMF	10 good
49*half (D)	1.0		MEK	(M)	1.0	DMF	12 good

(1) examples 42-45 and 49 used mineral oil in MEK.

(2) The catheters were soaked for 60 minutes and dried at 650C.

(3) The catheters were dipped for 1 second and dried at 650C.

* Entire catheter coated and coating sequence repeated.

TABLE III
PREPARATION AND EVALUATION OF
NYLON 11 CATHETERS

Example (1) Catheter Size cm (inch)	Primer Coating (2)		Top Coating (3)		Evaluation		
	Isocyanate	Weight (%) Solvent	Acid Compound	Weight %	Solvent	Abrasion lubricity	
50 10(4)	TDI	1.0	MEK	(M)	1.5	DMF/MEK (7:3)	15 (rubs) good
51 * 10(4)	TDI	1.0	MEK	(M)	1.5	DMF/MEK (7:3)	40 good
52 * 30(12)	TDI	1.0	MEK	(M)	1.0	Dioxane	15 very good
53 30(12)	TDI	1.0	MEK	(M)	1.0	Dioxane	10 very good
54 * 30(12)	TDI	1.0	MEK	(M)	1.0	DMF	35 very good
55 * 30(12)	TDI	1.0	MEK	(M)	1.0	DMF/MEK (7:3)	20 very good
56 30(12)	TDI	1.0	MEK	(M)	1.0	DMF	30 very good
57 30(12)	TDI	1.0	MEK	(M)	1.0	DMF/MEK (7:3)	15 very good

(1) Examples 56 and 57 were Nylon 12 catheters.

(2) The catheters were soaked for 60 minutes and dried at 85°C. except for Example 55 which soaked for 30 minutes.

(3) The catheters were dipped for 1 second and dried at 85°C.

* Coating sequence repeated with 60 minute primer soak and 10 minute top coat soak.

Example 58

A low viscosity, uniform colloidal dispersion of poly(acrylic acid) (N) was prepared by the following procedure: Into a 2-liter stainless steel reactor, equipped with a turbine agitator, condenser, thermometer, and an exterior heating bath, there was charged under agitation 487.17 grams of DMF (Mallinckrodt), 252.7 grams of MEK (Mallinckrodt), 234.3 grams of tertiary butyl alcohol (Arco), and 0.83 grams of MYRJ®-53 (an ethoxylated stearic acid produced by ICI). Once a uniform solution was obtained, 25 grams of poly(acrylic acid) (N) powder were introduced by pouring directly into the reactor. The reactor was heated to 50°C and maintained at $50 \pm 2^\circ\text{C}$ for one hour while under agitation at 2000 rpm. Thereafter, the reactor was cooled to room temperature and the content was transferred into a Waring Blender for homogenization. The homogenized product was filtered through a 10 μm polypropylene filter cartridge to yield a uniform colloidal dispersion. It showed the following viscosity properties:

Before homogenization	
Brookfield viscosity	40 mPa·s (centipoises)
Kinematic viscosity	17.3 mm ² /s (centistokes)
After homogenization	
Brookfield viscosity	7 mPa·s (centipoises)
Kinematic viscosity	8.7 mm ² /s (centistokes)

Example 59

A primer solution was prepared by mixing 80.91 parts of MEK (Mallinckrodt), 15.47 parts of mineral oil (Mallinckrodt), 3.6 parts of polyisocyanate E and 0.02 parts of FLUORAD® 431 (a surfactant produced by 3M) to yield a mobil, clear liquid. The solution contained 0.84% by weight of isocyanate groups.

Example 60

This example illustrates the preparation of a sodium phosphate solution for the acid neutralization of the poly(carboxylic acid) coating of this invention.

An 0.1 N sodium phosphate solution was prepared by dissolving 13.8 grams of the reagent (Matheson, Coleman & Bell) into one liter of distilled water. Separately, an 0.1N disodium phosphate solution was made by mixing 7.1 grams of the reagent (Matheson, Coleman & Bell) into one liter of distilled water. Into a one liter beaker containing about 660 ml of the 0.1N disodium phosphate solution, there was added under mixing a sufficient amount of the 0.1N sodium phosphate solution until the pH reached 7.

Example 61

A plasticized styrene-butadiene catheter was coated according to the following process to yield durable lubricious coating of this invention.

A 37.5 cm (15 inch) long catheter was dipped for 1 minute in a stainless steel bath containing the primer of Example 59. The coated catheter was air dried briefly and followed by baking in a forced air oven at 85°C for 30 minutes. The primed catheter was dipped quickly in a topcoat bath containing the polyacrylic acid colloidal dispersion of Example 58. Following a brief air-drying the wet catheter was dried in the oven at 85°C for 60 minutes. A uniform coating was produced, which became lubricious instantly upon exposure to water. The coating exhibited a good adhesion to the catheter.

Example 62

This example illustrates the utility of post neutralization for preserving hydrophilic lubricity of the coated catheter during a thermoforming process.

A plasticized polystyrene-butadiene catheter coated according to Example 61 was dipped in a bath containing the sodium phosphate solution of Example 60. The treated catheter was air dried for one hour, thereafter the catheter was shaped and heated in that shape at 120°C for 90 minutes. The finished shaped catheter became lubricious instantly upon exposure to water.

Example 63

The thermoforming treatment of Example 62 was repeated without first dipping in the sodium phosphate solution.

The finished stem was no longer lubricious upon exposure to water.

Example 64

This example illustrates the preparative procedure for producing a top coat dispersion containing a poly(methacrylic acid) polymer.

Into a one-liter size Pyrex® glass reactor equipped with a turbine agitator, a thermometer, a condenser, an external heating bath and an addition funnel there was charged 312 grams of DMF, 120 grams of t-butyl alcohol, 158.7 grams of MEK, 0.3 grams of MYRJ®-53 surfactant and 9 grams of poly(methacrylic acid) (Polysciences). The mixture was heated to 50°C while under vigorous mixing. After a 1 hour mixing, a uniform solution was obtained. The dispersion was cooled to room temperature and its viscosity measured with a Brookfield Model LVT Viscometer. The value was 5 mPa-s (centipoises).

Example 65

The same thermoplastic rubber catheter used in Example 42 was coated with the polyisocyanate primer (E) and the poly(methacrylic acid) top coat solution prepared in Example 64 according to the following procedure:

1. One minute dip in the primer solution.
2. One minute air dry and followed by a 30 minute bake in a 85°C forced-air oven.
3. One second dip in the poly(methacrylic acid) top coat dispersion.
4. One minute air drain followed by a 60 minute bake in a 85°C forced-air oven.

The finished catheter was lubricious upon contacting with water.

Example 66

Example 65 was repeated with the exception that a Nylon 11 catheter was used instead of the thermoplastic rubber catheter. The coated catheter was lubricious upon contact with water.

Example 67

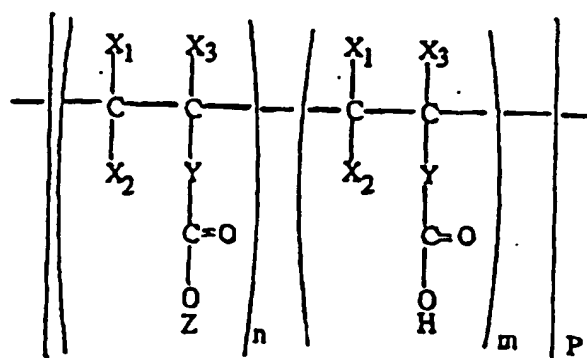
This example illustrates the utility of a spray coating process for producing the lubricious coating of the invention.

A group of four thermoplastic rubber catheters were cut to a length of 45 cm (18 inches) and mounted on steel mandrels. The latter were mounted on a steel stand inside a ventilated hood. The polyisocyanate primer (E) was sprayed onto the catheters using an air-spray gun(The Devilbiss Co., Toledo, Ohio, Type JGA-502). After a 30 minute baking at 85°C in a forced-air oven, the primed catheters were sprayed with a coat of poly(methacrylic acid) top coat (N). After a 60 minute baking, a fairly smooth coating was obtained. The coated catheters became lubricious immediately upon exposure to water.

Claims

1. A method of covering at least a portion of a substrate with a hydrophilic coating having good abrasion resistance and which exhibits an increased lubricity when contacted with an aqueous-containing fluid, said method comprising the steps of:

- (1) contacting said substrate with a polyisocyanate or end-capped prepolymer or adduct thereof dissolved or dispersed in at least one first inert solvent to provide an at least partially coated substrate;
- (2) contacting said coated substrate with a poly(carboxylic acid) polymer of the formula:



where

- $n =$ 0-0.95 mole fraction of neutralized acid moieties;
 $m =$ 0.05-1.0 mole fraction of acid moieties with the proviso that $n+m=1$;
 X_1, X_2, X_3 are each a hydrogen atom or a monovalent organic radical;
 Y is a single bond or a divalent organic radical;
 Z is a metallic ion or a tertiary ammonium ion; and
 P is a number such that the polymer has a molecular weight between 200,000 and 5,000,000;
 said poly(carboxylic acid) polymer dissolved or dispersed in at least one second solvent which is not reactive with the polyisocyanate component employed in step (1) to provide a multiple coated substrate; and

(3) thereafter drying said multiple coated substrate to provide a hydrophilic, lubricious coating.

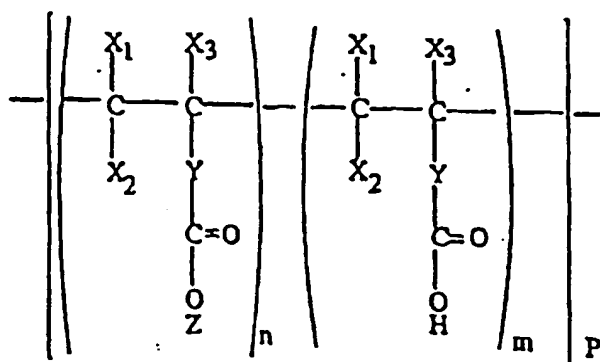
2. The method of claim 2 wherein said substrate is a medical device, e.g. a catheter.
3. The method of at least one of the claims 1 to 2 wherein said polyisocyanate is a diisocyanate.
4. The method of at least one of the claims 1 to 3 wherein said coated substrate is thermoformed to different shapes.
5. The method of at least one of the claims 1 to 4 wherein at least one additive is incorporated into said coated substrate.
6. The method to claim 5 wherein said additive is an antithrombogenic agent, e.g. heparin.
7. The method of at least one of claims 1 to 6 wherein said first solvent is selected from methyl ethyl ketone, ethyl acetate, ethyl lactate, chloroform, trichloroethylene, dichloromethane, hexane, heptane, toluene and their mixtures with mineral oil.
8. The method of at least one of claims 1 to 6 wherein said second solvent is selected from acetonitrile, DMF (N,N-dimethyl formamide), acetonitrile-DMF, acetyl acetone, acrylonitrile, benzonitrile, diethyl acetamide, diethyl formamide, diethyl formamide-DMF, dimethyl acetamide, 1,4-dioxane, dipropyl sulfone, DMF-acetone, DMF-toluene, DMSO (dimethyl sulfoxide), DMSO-DMF, ethyl formamide, N-methyl-2-pyrrolidone, nitrobenzene, nitrobenzene-DMF, phenylacetate, propionitrile, styrene, DMF-MEK (methyl ethyl ketone), dioxane and MEK-t-butyl alcohol.

Patentansprüche

1. Verfahren zur Bedeckung mindestens eines Teils eines Substrats mit einem hydrophilen Überzug mit guter Abriebbeständigkeit, der eine erhöhte Gleitfähigkeit aufweist, wenn er mit einem wasserhaltigen Fluid in Kontakt gebracht wird, wobei das Verfahren die folgenden Schritte umfaßt:

(1) Kontaktieren des Substrats mit einem Polyisocyanat oder einem mit Endgruppe abgeschlossenen Prepolymer oder Addukt davon, das in mindestens einem ersten inerten Lösungsmittel gelöst oder dispergiert ist, um ein zumindest teilweise beschichtetes Substrat bereitzustellen;

(2) Kontaktieren des beschichteten Substrats mit einem Poly(carbonsäure)-Polymer der Formel:



world

n = 0 - 0,95 Molfraktion von neutralisierten Säure-Einheiten;

$m =$ 0,05 - 1,0 Molfraktion von Säure-Einheiten mit der Maßgabe, daß $n + m = 1$:

X_1, X_2, X_3 jeweils ein Wasserstoffatom oder einen einwertigen organischen Rest darstellen;

Y eine Einfachbindung oder ein zweiwertiger organischer Rest ist;

Z ein metallisches Ion oder ein tertiäres Ammoniumion ist; und

P eine solche Zahl ist, daß das Polymer ein Molekulargewicht zwischen 200000 und 5000000 aufweist:

wobei das Poly(carbonsäure)-Polymer in mindestens einem zweiten Lösungsmittel, das mit der in Stufe (1) eingesetzten Polyisocyanat-Komponente nicht reaktiv ist, gelöst oder dispergiert ist, um ein mehrfach beschichtetes Substrat bereitzustellen; und

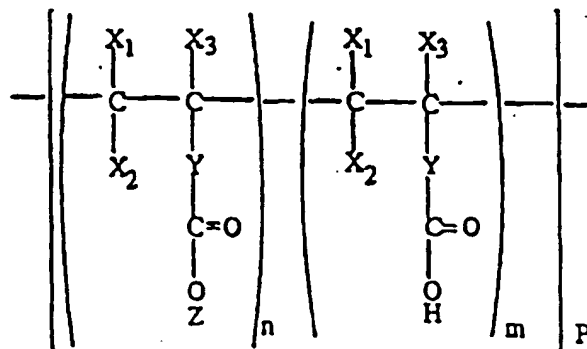
(3) anschließende Trocknung des mehrfach beschichteten Substrats unter Bereitstellung eines hydrophilen, gleitfähigen Überzugs.

2. Verfahren nach Anspruch 1, in welchem das Substrat eine medizinische Vorrichtung, z.B. ein Katheter, ist.
3. Verfahren nach mindestens einem der Ansprüche 1 bis 2, in welchem das Polyisocyanat ein Diisocyanat ist.
4. Verfahren nach mindestens einem der Ansprüche 1 bis 3, in welchem das beschichtete Substrat einer Wärmeformung zu unterschiedlichen Gestalten unterzogen wird.
5. Verfahren nach mindestens einem der Ansprüche 1 bis 4, in welchem mindestens ein Additiv in das beschichtete Substrat einverleibt wird.
6. Verfahren nach Anspruch 5, in welchem das Additiv ein antithrombogenes Mittel, beispielsweise Heparin, ist.
7. Verfahren nach mindestens einem der Ansprüche 1 bis 6, in welchem das erste Lösungsmittel aus Methylethylketon, Ethylacetat, Ethyllactat, Chloroform, Trichlorethylen, Dichlormethan, Hexan, Heptan, Toluol und deren Mischungen mit Mineralöl ausgewählt wird.
8. Verfahren nach mindestens einem der Ansprüche 1 bis 6, in welchem das zweite Lösungsmittel aus Acetonitril, DMF (N,N-Dimethylformamid), Acetonitril-DMF, Acetylaceton, Acrylnitril, Benzonitril, Diethylacetamid, Diethylformamid, Diethylformamid-DMF, Dimethylacetamid, 1,4-Dioxan, Dipropylsulfon, DMF-Aceton, DMF-Toluol, DMSO (Dimethylsulfoxid), DMSO-DMF, Ethylformamid, N-Methyl-2-pyrrolidon, Nitrobenzol, Nitrobenzol-DMF, Phenylacetat, Propionitril, Styrol, DMF-MEK (Methylethylketon), Dioxan und MEK-t-Butylalkohol ausgewählt wird.

Revendications

1. Procédé pour recouvrir au moins une partie d'un substrat d'un revêtement hydrophile ayant une bonne résistance à l'abrasion et présentant une capacité de glissement accrue au contact d'un fluide aqueux, ce procédé comprenant les étapes consistant :

(1) à faire entrer le substrat en contact avec un polyisocyanate ou un prépolymère à coiffe terminale ou un produit d'addition de ce polyisocyanate en solution ou en dispersion dans au moins un premier solvant inerte pour obtenir un substrat au moins partiellement revêtu ; (2) à faire entrer ce substrat revêtu en contact avec un polymère du type poly(acide carboxylique) de formule :



dans laquelle

- \underline{n} = 0-0,95 est la fraction molaire de groupements acides neutralisés ;
 \underline{m} = 0,05-1,0 est la fraction molaire de groupements acides, sous réserve que la somme $n+m$ soit égale à 1 ;
 X_1, X_2, X_3 représentent chacun un atome d'hydrogène ou un radical organique monovalent ;
 Y est une liaison simple ou un radical organique divalent ;
 Z est un ion métallique ou un ion ammonium tertiaire ; et
 P est un nombre tel que le polymère ait un poids moléculaire compris entre 200 000 et 5 000 000 ; le polymère du type poly(acide carboxylique) en question étant dissous ou dispersé dans au moins un second solvant qui n'est pas réactif envers le composant polyisocyanate utilisé dans l'étape (1) en vue d'obtenir un substrat à revêtement multiple ; et

(3) à sécher ensuite le substrat à revêtement multiple pour obtenir un revêtement hydrophile glissant.

2. Procédé suivant la revendication 1, dans lequel le substrat est un dispositif médical, par exemple un cathéter.
3. Procédé suivant l'une au moins des revendications 1 et 2, dans lequel le polyisocyanate est un diisocyanate.
4. Procédé suivant l'une au moins des revendications 1 à 3, dans lequel on fait prendre par thermoformage différentes formes au substrat revêtu.
5. Procédé suivant l'une au moins des revendications 1 à 4, dans lequel au moins un additif est incorporé au substrat revêtu.
6. Procédé suivant la revendication 5, dans lequel l'additif en question est un agent antithrombogénique, par exemple l'héparine.
7. Procédé suivant l'une au moins des revendications 1 à 6, dans lequel le premier solvant est choisi entre la méthyléthylcétone, l'acétate d'éthyle, le lactate d'éthyle, le chloroforme, le trichloréthylène, le dichlorométhane, l'hexane, l'heptane, le toluène et leurs mélanges avec une huile minérale.
8. Procédé suivant l'une au moins des revendications 1 à 6, dans lequel le second solvant est choisi entre l'acétonitrile, le DMF (N,N-diméthylformamide), le mélange acétonitrile-DMF, l'acétylacétone, l'acrylonitrile, le benzonitrile, le diéthylacétamide, le diéthylformamide, le mélange diéthylformamide-DMF, le diméthylacétamide, le 1,4-dioxanne, la dipropylsulfone, le mélange DMF-acétone, le mélange DMF-toluène, le DMSO (diméthylsulfoxyde), le mélange DMSO-DMF, l'éthylformamide, la N-méthyl-2-pyrrolidone, le nitrobenzène, le mélange nitrobenzène-DMF, l'acétate de phényle, le propionitrile, le styrène, le mélange DMF-MEK (méthyléthylcétone), le dioxanne et le mélange MEK-alcool tertio-butylque.

THIS PAGE BLANK (USPTO)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.

THIS PAGE BLANK (USPTO)